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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/31/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,341	FORMAN ET AL.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *94,95,103-109 and 111* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *94,95,103-109 and 111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/29/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 4/29/2004 is acknowledged. Claims 96-102 and 110 are canceled.

2. Claims 94, 95, 103-109 and 111 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn:

4. The rejection of claim 110 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the cancellation of claim 110.

5. The rejection of claims 94, 104-110 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment to claim 94.

6. The rejection of claim 110 under 35 U.S.C. 102(e) as being anticipated by Shtil (U.S. Patent 6,71,786; issued Jan. 9, 2001; effective filing date June 7, 1996) is withdrawn in view of the cancellation of claim 110.

New Grounds of Rejection:

7. Claims 94, 95, 103-109 and 111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 94 is indefinite, as are any claims that depend from claim 94, because the phrase "functional analog of Ecteinascidin-743" is undefined. Therefore, the scope of the claims is undefined. Without a definition in the specification, it is not clear if the claimed methods are drawn to methods for identifying which structural analogs of Ecteinascidin-743 have the same or similar function as that of Ecteinascidin-743, or if the claimed methods are drawn to methods for identifying whether any compound, whether a structural analog or not of Ecteinascidin-743, has the same or similar function as that of Ecteinascidin-743. This affects the scope of the claimed inventions because it affects the scope of what are appropriate test compounds. Additionally, claim 94 is indefinite because of the recitation of step "b", determining whether a test compound inhibits steroid and xenobiotic receptor (SXR) transactivation of mdr1 and cyp3a4. This is because it is not clear if step "b" is limited to assays where transactivation of mdr1 or cyp3a4 is tested by specifically testing for SXR involvement in mdr1 or cyp3a4 transactivation or if step "b" includes assays where SXR involvement is merely assumed and effects of compounds on mdr1 or cyp3a4 mRNA expression is measured directly.

Claim 106 is indefinite because the phrase "the SXR ligand binding domain" lacks antecedent basis in claim 104 or 94, from which claim 106 depends.

Claim 111 is indefinite because the phrase "said determining whether said test compound inhibits SXR trans activation of an SXR target gene" lacks antecedent basis in claim 94, from

which claim 111 depends. This rejection would be obviated by an amendment changing the phrase "said determining whether said test compound inhibits SXR trans activation of an SXR target gene" to the following "said determining whether said test compound inhibits SXR trans activation of mdr1 or cyp3a4".

8. Claims 94, 95, and 103-109 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the amendment to claim 94 appears to introduce new matter into the specification.

The amendment to claim 94 limits the scope of the SXR target genes to mdr-1 and cyp3a4. Applicant does not point to any passages in the disclosure of the specification for support for this amendment, but instead points to a non-patent literature reference that has been incorporated by reference. This is not sufficient support for the amendment to claim 94. Applicant is reminded that incorporation by reference of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Furthermore, the amendment to claim 94 changes the scope of the invention to a scope that does not appear to have been originally contemplated at the time of filing.

9. Claim 108 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in

the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the specification fails to describe the genus of peptides that are SXR coactivator mimetic peptides.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is for purposes of the 'written description' inquiry, "*whatever is now claimed*" (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now claimed." (See Vas-Cath at page 1116.)

In the instant case, the originally filed claims recite the phrase "a mimetic peptide which is a coactivator of SXR", however, such a recitation does not constitute a description of such peptides and appears to be nothing more than a contemplation to use such peptides in the claimed methods. What is lacking from the specification is description of the structure of any example of such a peptide.

The skilled artisan cannot envision the detailed chemical structure of the encompassed by the phrase "SXR coactivator mimetic peptide" used in the method claims and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of manufacturing or testing the claimed process. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making or testing it. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian

FGF's were found unpatentable due to lack of written description for the broad class. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112, is severable from its enablement provision. (See page 1115).

10. Claims 94, 104-109 and 111 are rejected under 35 U.S.C. 102(b) as being anticipated by Evans (WO 99/35246; published 15 July 1999).

Claims 94, 104-109 and 111 are drawn to method for screening for compounds that inhibit SXR transactivation of a target gene (claim 111 is not limited to mdr-1 or cyp3a4 as the target gene, but is dependent from claim 94). The methods may comprise measuring the effect of a test compound on expression of a reporter construct.

Evans teaches and claims a method for testing a compound for its ability to regulate transcription-activating effects of an SXR receptor, comprising assaying for the presence or absence of reporter protein upon contacting cells containing a reporter gene construct (see page 52, claim 23). Evans also teaches that SXR activates cyp3a4 transcription (page 34, line 24 – page 35, line 22). Therefore, Evans teaches methods that are the same as that claimed.

11. Claims 94, 95, and 103-109 are rejected under 35 U.S.C. 102(e) as being anticipated by Chaudhary (U.S. Patent 5,972,598; effective filing date Jan. 10, 1995).

The claimed inventions are drawn to methods comprising determining whether said test compound inhibits steroid and xenobiotic (SXR) transactivation of an SXR target gene selected from the group consisting of mdr-2 and cyp3a4. The claimed methods may be used to identify a functional analog of Ecteinascidin-743 (Ect-743) that inhibits drug-resistance, to identify a

functional analog of Ect-743 that inhibits the ability of SXR to transactivate mdr1 gene transcription, to identify an analog of Ect-743 that is an SXR antagonist, to identify an SXR antagonist that prevents displacement of an SXR corepressor from SXR, to identify an SXR antagonist that prevents binding of an SXR ligand to an SXR ligand binding domain, to identify an SXR antagonist that inhibits interaction between SXR and an SXR coactivator, to identify an SXR antagonist that inhibits interaction between SXR and SRC1, ACTR, GRIP, PBP or an SXR coactivator mimetic peptide, or the method may be used to identify an SXR antagonist that is cytotoxic to tumor cells.

Chaudhary teaches a method of measuring the inhibition by protein kinase inhibitors of drug-induced mdr-1 mRNA synthesis (see abstract and col. 19, line 50 – col. 20, line 13). Therefore, Chaudhary teaches a method that identifies whether a compound inhibits SXR transactivation of mdr-1, because Chaudhary demonstrates examples of protein kinase inhibitors that inhibits drug induction of mdr-1 mRNA synthesis. Because the claims are broadly drawn to methods comprising a step for determining whether a test compound inhibits SXR transactivation of mdr-1, without a recitation of actual measurements that are to be made, and because an inhibition of transacivation will result in a decrease in mRNA synthesis, Chaudhary's method comprises step (b) of the claims. Therefore, Chaudhary teaches methods that are the same as that claimed.

12. Claims 94, 95, and 103-109 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jin (Jin, S. et al. Proc. National Acad. Sci., USA, 97(12): 6775-6779, 2000, June 6) in view of Martinez (Martinez, E.J., Proc. Natl. Acad. Sci., USA, 96: 3496-3501, 1999, March).

The claimed inventions are drawn to methods comprising determining whether said test compound inhibits steroid and xenobiotic (SXR) transactivation of an SXR target gene selected from the group consisting of mdr-2 and cyp3a4. The claimed methods may be used to identify a functional analog of Ecteinascidin-743 (Ect-743) that inhibits drug-resistance, to identify a functional analog of Ect-743 that inhibits the ability of SXR to transactivate mdr1 gene transcription, to identify an analog of Ect-743 that is an SXR antagonist, to identify an SXR antagonist that prevents displacement of an SXR corepressor from SXR, to identify an SXR antagonist that prevents binding of an SXR ligand to an SXR ligand binding domain, to identify an SXR antagonist that inhibits interaction between SXR and an SXR coactivator, to identify an SXR antagonist that inhibits interaction between SXR and SRC1, ACTctR, GRIP, PBP or an SXR coactivator mimetic peptide, or the method may be used to identify an SXR antagonist that is cytotoxic to tumor cells.

Jin teaches a method of measuring the inhibition by Ect-743 of drug-induced mdr-1 mRNA synthesis. The drugs used to induce mdr-1 synthesis were trichostatin-A (TSA) and butyrate (see page 6776, Fig. 1). Therefore, Jin teaches a method that identifies Ect-743 as a compound that inhibits SXR transactivation of mdr-1, because Jin demonstrates that Ect-743 inhibits mdr-1 mRNA synthesis, which one would expect from a compound that inhibits SXR transactivation of mdr-1. Because the claims are broadly drawn to methods comprising a step for determining whether a test compound inhibits SXR transactivation of mdr-1, without a recitation of actual measurements that are to be made, and because an inhibition of transacivation will result in a decrease in mRNA synthesis, Jin's method comprises step (b) of the claims.

Jin fails to teach screening for other compounds that, like Ect-743, will inhibit a drug-induced increase in mdr-1 mRNA levels. However, Martinez teaches the existence of drugs that have structural similarity to Ect-743 and have similar levels of anti-tumor activity. Martinez also teaches that Ect-743 is a rare natural product and that supplies of Ect-743 are inadequate for large scale studies. Martinez teaches that compounds, such as phthalascidin (Pt-650), have been developed that are structural relative of Ect-743.

Therefore, in view of the motivation to discover more compounds that share the anti-tumor activity of Ect-743, it would be prima facie obvious to one of ordinary skill use the methods of Jin to screen compounds taught by Martinez, such as Pt-650, to discover if such compounds inhibit drug induced increase in mdr-1 mRNA levels.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran
Patent Examiner
August 30, 2004

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER
8/30/2004